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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,560	12/08/2000	Robert Schlegel	MRI-008A	3311

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EXAMINER	
SMITH, CAROLYN L	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/732,560	SCHLEGEL ET AL.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2003 and 30 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *4,20-37 and 39-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-19, and 38* is/are rejected.

7)☒ Claim(s) *1-3,5-19 and 38* is/are objected to.

8)☒ Claim(s) *1-46* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' election without traverse of Group I (claims 1-23 and 38) and sequence election of SEQ ID NO: 100, filed 4/15/03 and 7/30/03, is acknowledged. Claims 24-37 and 39-46 are withdrawn from consideration as being drawn to non-elected Groups. Claim 4 is withdrawn as being drawn to Tables containing non-elected sequences. Claims 20-23 are withdrawn as the election to a single marker does not include the evaluation of a plurality of markers as required in claims 20-23.

The amendment of Table 8B and the paragraph starting on page 27, line 29, is acknowledged and satisfies sequence compliance rules.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed to compositions, kits, methods for identification, assessment, prevention, and therapy of cervical cancer, whereas in contrast the elected claim is specifically directed to a method and kits for assessment of cervical cancer.

Claims herein under examination are 1-3, 5-19 and 38.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, such as on page 38, line 10; page 87, line 16; and elsewhere. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claims 1-3, 5-19, and 38 are objected to due to the inclusion of subject matter which has been non-elected due to a restriction requirement and therefore withdrawn from consideration. The non-elected subject matter in claims 1-3, 5-19, and 38 is summarized as follows: Claim 1 recites the phrase "wherein the marker is selected from the group consisting of the markers listed in Tables 1-13" whereas only SEQ ID NO: 100 (from Table 8B) is elected. Claims 2-3 and 5-19 are also rejected due to their direct or indirect dependency from claim 1. Claim 38 recites the phrase "a marker selected from the group consisting of the markers in Tables 1-13" whereas only SEQ ID NO: 100 (from Table 8B) is elected. Removal of withdrawn material from the claims is requested.

Claim 9 is objected to due to the minor informality: the word "an" on line 3 is improper as the word it precedes begins with a consonant. Appropriate correction is requested.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The

factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

LACK OF SCOPE OF ENABLEMENT

Claims 1-3 and 5-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain aspects of assessing cervical cancer or a pre-malignant condition for cervical tissue, does not reasonably provide enablement for such an assessment with any type of tissue. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In claim 1, the pre-malignant condition limitations are seemingly applicable to any tissue. However, the specification only provides enablement for utilizing the elected marker for assessing a pre-malignant condition for cervical tissue, such as cervical intraepithelial neoplasia or squamous intraepithelial lesions (page 7, sixth paragraph).

LACK OF ENABLEMENT

Claims 5, 10-12, 17, and 38 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 5 and 10-12 are directed to a marker that corresponds to a protein. However, it is noted that SEQ ID NO: 100 is only 471 nucleotides long, which is a fairly short sequence. The specification does not appear to state what protein corresponds to SEQ ID NO: 100 in order to enable these claims.

Claims 17 and 38 are directed to marker assessment wherein annealing to a portion of the marker or a probe directed to binding to a marker polynucleotide is utilized. Such portion or probe limitations are enabled only via hybridization probe selection methodology. Such methodology is well known for defining a hybridization probe with conditions which will hybridize to a target marker polynucleotide but is not well defined as to what specificity is required for detecting a marker where similar markers may and usually are present. This specificity enablement requires careful determination of negative control nucleic acids. The specification does not appear to have any enabling discussion as filed for what negative controls are needed to enable the above discussed hybridization probe use. Shah et al. (P/N 5,521,300) provide an example of a disclosure wherein the need for appropriate negative control nucleic acids is described when hybridization probes which are useful are determined (col. 2-9, especially col. 7, lines 51-67). Shah et al. demonstrate the unpredictability of hybridization probe design without defining a set of appropriate negative controls. Therefore, claims 17 and 38 are rejected for a lack of enablement.

LACK OF WRITTEN DESCRIPTION

Claims 1-3, 5-19, and 38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the invention was filed, had possession of the claimed invention.

Claims 1 and 38 include elected SEQ ID NO: 100 which is listed in amended Table 8B as "SEQ ID NO: 3559: found in patent publication WO 99/46375." An actual copy of this WO publication reveals that it only has sequences up to SEQ ID NO: 295. This raises the question of how the sequence can then be described in Table 8B with SEQ ID NO: 3559 in such a WO publication when no such SEQ ID NO exists.

The specification discloses SEQ ID NO: 100 which corresponds to nucleic acid sequence. SEQ ID NO: 100 and its full-length complement meet the written description provisions of 35 U.S.C. 112, first paragraph. However, claims 6, 13-17, and 38 are directed to encompass portions, including a probe (claim 38), of SEQ ID NO: 100 which do not meet the written description provision of 35 U.S.C. 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by these claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 100, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable

due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only SEQ ID NO: 100 and its full-length complement, but not the full breadth of the claims 6, 13-17, and 38, meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Claims Rejected Under 35 U.S.C. § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 and 5-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

In claim 1, the preamble seems to be inclusive of any tissue where a pre-malignant condition is being assessed. Confusingly, in part b) of claim 1, the expression normal level seems to be defined by a control non-cervical cancer sample. It is unclear what is meant by comparing any cancerous pre-malignant condition to a particular control such as non-cervical cancer. Clarification of this issue is requested. Claims 2-3 and 5-19 are also rejected due to their direct or indirect dependency from claim 1.

Claim 1 (lines 5-6) recites the phrase "control non-cervical cancer sample" which is vague and indefinite. It is unclear if the control is a cervical sample which is non-cancerous or if it is a cancer sample from a non-cervical sample. Clarification of the metes and bounds via clearer claim wording is requested. Claims 2-3 and 5-19 are also rejected due to their direct or indirect dependency from claim 1.

Claims 2 and 3 are vague and indefinite due to the unclarity of citing an abbreviation, such as CIN and SIL. Correction is suggested by amending in of the full name in parentheses.

Claim 8 recites the limitation "the sample". There is insufficient antecedent basis for this limitation in the claim. It is unclear if "the sample" is referring to the patient sample in part a) or the control non-cervical cancer sample in part b). Clarification of this issue via clearer claim wording is requested.

Claim 12 recites the phrase "antibody derivative" which is vague and indefinite. It is unclear what the metes and bounds are for this type of derivative. Clarification of the metes and bounds of this phrase via clearer claim wording is requested.

Claim 17 recites the phrase "under stringent hybridization conditions" which is vague and indefinite. It is unclear which criteria the applicants regard as stringent conditions (i.e. buffers,

pH of buffer, etc.) or whether low, medium, or high stringency is meant. Applicants can resolve this issue by particularly pointing out the stringent conditions that are intended to allow the polynucleotide to hybridize. Clarification of the metes and bounds of the instant claims is required.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (703) 308-6043. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

October 8, 2003

ARDIN H. MARSCHEL
PRIMARY EXAMINER